REMARKS

Status of the claims

Claims 1-34 are pending and claims 1-18 are presently under consideration in this application, claims 19-34 having been withdrawn from consideration on the ground that they are drawn to separate inventions. All the claims presently under consideration stand rejected. After entry of the amendments made herein, claims 1-54 will be pending and claims 1-18 and 35-54 will be under consideration in this application, claims 35-54 having been added herein. Support for amendments to claims 3, 4, 9, and 10, which add no new matter, can be found in the specification, e.g., at page 2, lines 28-31. Newly added claims 35-54, which are supported throughout the specification and the claims as originally filed, add no new matter. Amendments to conform some of the claims to U.S. patent style and/or to enhance clarity have been made and these amendments also add no new matter.

Specification

The above amendments to the specification serve: (a) to correct the informality pointed out by the Examiner on page 2, paragraph 3, of the Office Action; and (b) to replace citations to U.S. Application Serial No. 08/796,792 with citations to U.S. Patent No. 6,087,163, which issued from U.S. Application Serial No. 08/796,792.

35 U.S.C. §112, first paragraph, rejections

(a) Claims 1-18 stand rejected on the grounds that the specification allegedly does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims. Applicant respectfully traverses the rejection.

From the comments on page 3, lines 1-12, of the Office Action, Applicant understands the Examiner's position to be that, because the experiment described in Example 1 was only performed using MTBN4, DNAs encoding MTBN1-3 and MTBN5-8 are not enabled by the specification. Applicant respectfully disagrees with this position.

Applicant understands the Examiner to be questioning whether the MTBN proteins (other than MTBN4) exhibit antigenic and immunogenic properties. The experiment described in Example 1 was performed to test whether testing for immunoreactivity to MTBN4 could discriminate between exposure to *M. tuberculosis* and exposure to BCG. It was not designed to test whether MTBN4 had antigenic or immunogenic properties (as defined on page 7, lines 8-22, of the instant specification), properties of the MTBN proteins required by the instant claims. Indeed, because MTBN4 (like all the other MTBN proteins disclosed in the present application) is a bacterial protein, a person skilled in the art would expect, as Applicant expected, that it, and all the other MTBN proteins, would indeed have immunogenic properties in a mammal such as a guinea pig, e.g., would elicit the production of antibodies by the guinea pig. Moreover, Applicant expected, as persons skilled in the art would expect, that all the MTBN proteins would have antigenic properties, e.g., would be recognized by (and hence bind to) appropriately specific antibodies.

Applicant respectfully submits that persons skilled in the art would similarly expect the MTBN proteins to have such immunogenic and antigenic properties and, hence, there is no adequate basis for an enablement (or utility) rejection (*In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995)). In this case the Examiner has not met the USPTO's burden of setting forth a reasonable explanation for doubting the objective truth of statements by Applicant. (*Fiers v. Revel*, 984 F.2d 1164 (Fed. Cir. 1992); *In re Wright*, 999 F.2d 1587 (Fed. Cir. 1993))

While not necessary to support the above argument for enablement, Applicant has performed experiments that incidentally support the argument. These experiments, which showed that all of four randomly selected MTBN proteins (in addition to MTBN4) have immunogenic and antigenic properties as defined by the present specification, were described in an article (Brusasca et al., Scand. J. Immunol. 54:448-452, 2001), a copy of which is enclosed as Exhibit A. The experiments depicted in Figures 1 and 2 of the article show that MTBN1 ("Rv3871"), MTBN2 ("Rv3872"), MTBN3 ("Rv3873"), MTBN4 ("MTSA-10"), and MTBN7 ("Rv3878") have both immunogenic and antigenic properties. The data presented in Figure 1 indicate that all these MTBN proteins (in the *M. tuberculosis* used to sensitize the experimental

guinea pigs) stimulated antigen-specific T cells (which mediate delayed-type hypersensitivity) and that these antigen-specific T cells recognized and responded to the MTBN proteins when the respective guinea pigs were challenged with the them. The results depicted in Figure 2 indicate that the MTBN proteins (in the *M. tuberculosis* used to sensitize the experimental guinea pigs) elicited the production of antibodies in the most test animals and that these antibodies recognized and bound to the relevant MTBN proteins.

In addition, another research group tested for and found in sera from tuberculosis patients and *M. tuberculosis*-infected mice antibodies specific for ten *M. tuberculosis* proteins (Daugelet et al., Microbes and Infection, 5:1082-1095, 2003; copy enclosed as Exhibit B; page 1092, column 1, paragraph 2, and Fig. 6). Importantly, antibodies specific for all the proteins tested were detected. Among these proteins were MTBN1 ("Rv3871"), MTBN2 ("Rv3872"), MTBN3 ("Rv3873"), MTBN4 ("CFP-10"), MTBN5 ("Rv3876"), MTBN7 ("Rv3878"), and MTBN8 ("Rv3879c"). While the authors of Daugelet et al. planned also to test for antibodies specific for MTBN6 ("Rv3877"), they had technical difficulties in purifying the relevant recombinant protein (see, e.g., page 1093, column 2, paragraph 2)) and so could not use it in their assays.

Thus, the experiments with the randomly selected proteins described in Brusaca et al. and Daugelet et al. provide support for the expectation that one of skill in the art would have regarding all the MTBN proteins specified by the instant claims, i.e., that they would have the requisite immunogenic and antigen properties. Assuming *arguendo* that the burden on enablement had shifted to Applicant, Applicant has more than met that burden. On the record as a whole, enablement is not in doubt.

(b) Claims 17 and 18 stand rejected on the grounds that the specification allegedly does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims.

From the comments on page 3, line 13, to page 4, line 5, of the Office Action, Applicant understands the Examiner's position to be that the present specification does not provide enablement for a method of determining the susceptibility of a subject to infection with *M.*

tuberculosis. While not necessarily agreeing with this position, in order to expedite prosecution of the present application, Applicant has amended claims 18 and 19 by substituting the phrase "subject has or is susceptible to *Mycobacteria tuberculosis* infection" with the phrase "subject has been exposed to *Mycobacteria tuberculosis*". This amendment, which is supported by the specification (e.g., at page 10, lines 24-26), adds no new matter and renders the rejection moot.

In light of the above considerations, Applicant respectfully requests that the rejections under 35 U.S.C. §112, first paragraph, be withdrawn.

CONCLUSIONS

Applicant submits that the pending claims patentably define the invention and request that the Examiner permit the pending claims to pass to allowance.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's undersigned representative can be reached at the telephone number listed below.

Enclosed is a request for an automatic extension of time and a check in payment of the extension in time. Also enclosed is a check in payment of excess claim fees. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 07763-043001.

Respectfully submitted,

Date: 12/23/03

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